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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/938,406	08/21/2001	George H. Lowell	40646-2000210	1965

20350 7590 11/16/2004

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,406	LOWELL ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *2 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-18 are pending in the application. In the prior action, mailed on April 5, 2004, claims 1, 3, 4, 6, 7, and 10-18 were under consideration and rejected, and claims 2, 5, 8, and 9 were withdrawn as to non-elected inventions. In the Response, filed on October 28, 2004, the Applicant amended claims 1, 3, 4, and 6-18. In view of the amendment of claims 8 and 9 as indicated by the Applicant, these claims are now considered part of the elected invention. Thus, claims 1, 3, 4, and 6-18 are under consideration, and claims 2 and 5 stand withdrawn as to non-elected inventions.

Specification

2. **(Prior Objection- Withdrawn)** The disclosure was objected to because of the following informalities: on page 6, line 3, the term "Atni-HIV" should read --anti-HIV--. In view of the amendment correcting the typographical error, the objection is withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. **(Prior Rejection- Maintained)** Claims 1, 3,4, 6, 7, 10-12, and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is now extended to claims 8 and 9. These claims read on compositions comprising an antigen and an

exogenous hydrophobic fatty acyl group or lauroyl material, and "a composition comprising proteosomes, bioadhesive nanoemulsions, or both, wherein said composition is complexed or coupled with (a)." The Applicant traverses the rejection by arguing that the composition is coupled or complexed with the antigen conjugate.

A "complex" is generally accepted to mean a combination of interrelated elements. See e.g., Merriam-Webster's Online Dictionary, 10th Ed. With reference to chemicals, it also implies some form of physical/chemical bond between the individual components. Id. Because the claims are requiring a complex between a composition and the antigens, and not between the nanomolecules or the proteosomes and the antigens within the compositions, it is unclear how the antigen is being complexed with the composition as a whole, rather than being complexed with the proteosomes or mixed with the bioadhesive emulsion, or complexed with a compound within the emulsion (see e.g., U.S. Patent 5,716,637, teaching that emulsions are "heterogeneous systems of one liquid dispersed in another," and teaching the incorporation of antigens into the emulsions). Clarification is required. Because it is unclear how a peptide can be "complexed" with a composition generally, rather than to elements within it, the rejection is maintained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **(Prior Rejection- Withdrawn)** Claims 1, 3, 4, 6, 7, and 10-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for vaccine compositions against certain pathogenic organisms (i.e. using vaccine antigens known in the art

to be effective), does not reasonably provide enablement for the full scope of the claims. The claims have been amended such that they now read on "immunogenic compositions" comprising the claimed antigen conjugates. In view of this amendment, the rejection is withdrawn.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. **(Prior Rejection- Maintained)** Claims 1, 3, 4, 6, and 10-17 were rejected under 35 U.S.C. 102(b) as being anticipated by Lowell et al., Science 240(4853): 800-02. The claims have been described above. The Applicant traverses the rejection by arguing (a) that the reference does not teach the inclusion of an "exogenous hydrophobic material in a composition with endogenous hydrophobic sequence as claimed," (b) that the reference fails to disclose or suggest the use of bioadhesive nanoemulsions, and (c) that the reference fails to "disclose or suggest the use of neutralizing antibodies." The arguments are not found persuasive.

With respect to (a) and (b), the claims are drawn to compositions comprising an antigen comprising a peptide having "(i) an endogenous hydrophobic sequence of between about 3 and, about 50 non-polar or uncharged amino acids;

(ii) added to the protein or peptide, an exogenous hydrophobic material comprising a sequence of between about 3 and about 50 non-polar or uncharged amino acids or a C8-C18 fatty acyl group; or

(iii) both (i) and (ii)," wherein the antigen is complexed to a proteosome, a bioadhesive nanoemulsion, or both.

Thus, the claims do not require the presence or both the endogenous hydrophobic sequence and the exogenous hydrophobic material in every embodiment. Nor does the claim require the presence of both compositions so long as either the proteosome composition or the bioadhesive nanoemulsion composition is present. The claim can therefore be anticipated by a reference that teaches only one from each set of alternatives. In this case, the reference teaches the conjugation of a synthetic peptide antigen to an exogenous lauroyl, and the conjugation of this conjugate to a proteosome. Page 800 middle column, and page 802, endnote 11. Because the claims do not require both of either set of alternatives to be present, the traversal is not found persuasive.

With respect to (c), it is noted that the antibodies referred to by Applicant are not part of the claimed invention, but rather are an intended result of their administration; the antibody induction language of the claim is read as an intended use of the claimed composition. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Thus, in the present case, Lowell will

be considered to anticipate the claims if the composition disclosed therein would be capable of use for the induction of mucosal antibodies.

As indicated above, the reference teaches all of the structural limitations of the claims. Additionally, the reference teaches antibodies against the epitope were induced by the administration of the disclosed vaccine, and that the epitope is a protective epitope. While the reference indicates that it did not specifically test for the ability of the antibodies to neutralize infection, the reference states that the antibodies possessed characteristics that were indicative of that ability. Page 801 right column, last full paragraph. These indications, in addition to teachings in the art indicating that the repeat sequence was a known protective epitope (see e.g. Zavala et al., J Exp Med 157: 1947-57) provides sufficient evidence that the antibodies disclosed therein were neutralizing, and thus that the is capable of inducing neutralizing antibodies. Further, because the reference teaches that composition induced neutralizing antibodies when administered to the animals, it appears that the composition would also be capable of inducing neutralizing mucosal antibodies. In view of the lack of any evidence to the contrary, and the lack of any structural distinction between the claims and the prior art, the rejection is maintained.

9. **(Prior Rejection- Maintained)** Claims 1, 3, 4, 6, and 10-17 were rejected under 35 U.S.C. 102(e) as being anticipated by Lowell et al., U.S. Patent 5,726,292 (the 292 patent). The claims have been described above. The Applicant has traversed this rejection on the same grounds as argued against the Lowell reference above. However, as the teachings of the 292 patent are substantially similar to those of the Lowell reference, the arguments are found no more persuasive against the rejection over the 292 patent. The Applicant has not pointed out any

structural differences between to compositions disclosed by the 292 patent and the claimed invention. For the reasons above, and the reasons of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **(Prior Rejection- Maintained)** Claims 7 and 18 were rejected under 35 U.S.C. 103(a) as being obvious over the 292 patent as applied against claims 1, 3, 4, 6, and 10-17 above. Claims 7 and 18 further limit the claimed constructs to embodiments wherein the protein antigen comprises a viral antigen or an antigen of a mucosally- or sexually transmitted disease. The Applicant traverses the rejection on the same grounds as argued against the anticipation rejection of claims 1, 3, 4, 6, and 10-17 over the 292 patent alone. For the reasons above, these arguments in traversal are not found persuasive, and the rejection is maintained.

12. **(Prior Rejection- Maintained)** Claims 7 and 18 were rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell as applied to claims 1, 3, 4, 6, and 10-17 above, and further in view of Vancott et al., J Immunol Methods 183: 103-17. Claims 7 and 18 have been described above.

The rejection is also expended to newly amended claim 8. These claims read on embodiments wherein the antigen comprises an oligomeric gp160 HIV protein, and particularly to a protein comprising residues 33-681 of SEQ ID NO: 1. The teachings of Vancott have been described in the prior action. The reference additionally reaches that the anti-HIV antigen disclosed therein is an oligomeric gp160 HIV protein. Thus, the reference also suggests the use of an antigen meeting the limitations of claim 8. The rejection is therefore extended to this claim.

The Applicant traverses this rejection on the same grounds as argued with respect to the Lowell reference above, and argues that the cited references do not discuss how to generate neutralizing mucosal antibodies. However, as was discussed above, the claims are drawn to the immunogenic compositions, and not to methods of making mucosal neutralizing antibodies, or to the antibodies themselves. As such, the neutralizing antibody language is considered as merely an intended use of the claimed invention. The arguments are therefore found no more persuasive with respect to claims 7 and 18 as they were with respect to the claims rejected over Lowell alone above. The rejection of claims 7 and 18 is therefore maintained for the reasons above and the reason of record.

13. **(Prior Rejection- Maintained)** Claims 1, 3, 4, 6, 7, 10, 11, 16-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over any of the 292 patent, Lowell, or Lowell in view of Vancott as applied above, and further in view of WO 95/11700. The rejection is further extended to amended claim 8 for the reasons indicated above. The Applicant traverses this rejection for the reasons argued with respect to the other rejections above, and argues that the WO 95/11700 reference does not remedy the deficiencies of the other references. These arguments are not

found persuasive for substantially the same reasons as indicated above. The rejection is therefore maintained.

14. **(New Rejection-Necessitated by Amendment)** Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell in view of Vancott as applied above, and further in view of Desai et al. (PNAS 83: 8380-84). Claim 9 reads on the subject matter of claim 8 as described above, wherein the oligomeric gp160 comprises the sequence of residues 33-681 of SEQ ID NO: 1. The teachings of Lowell and Vancott have also been described above. While these references teach the vaccine of claim 8, the Vancott reference does not teach the sequence of SEQ ID NO: 1. However, the teachings of the reference relate to the use of the gp160 protein in general, not to a specific version of the protein. Thus, it would have been obvious to those in the art to use any known gp160 protein in the oligomeric antigen. Desai teaches a gp160 protein sequence comprising the sequence of residues 33-681 of SEQ ID NO: 1. See, page 8382. It would therefore have been obvious to those in the art to use this gp160 to make the oligomeric gp160 as the anti-HIV antigen. The limitations of claim 9 are therefore obvious over the art.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. **(Prior Rejection-Maintained)** Claims 1, 3, 4, 6, 7, 10-18 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 7, and 8 of U.S. Patent No. 5,726,292. The Applicant traverses the rejection for the same reasons as argued with respect to the anticipation rejection above. These arguments are not found persuasive for the reasons indicated above. The rejection is therefore maintained.

17. **(New Rejection-Necessitated by Amendment)** Claims 1, 3, 4, 6, 7, 10-18 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 7, and 8 of U.S. Patent No. 5,726,292 further in view of Vancott and Desai as applied above. As indicated above, the teachings of the 292 patent are substantially similar to those of the Lowell reference. Thus, the combination of the cited claims with the teachings of Vancott and Desai would have rendered the compositions of claims 8 and 9 obvious for the same reasons as described in paragraphs 13 and 14 above.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 11/15/04
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